CLAIMS

1. A compound of formula (I):

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$$Ar - CHCH_2NHCR^4R^5(CH_2)_m - O - (CH_2)_n - R^2$$

$$OH$$

$$R^3$$
(I)

or a salt, solvate, or physiologically functional derivative thereof, wherein:

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m is an integer of from 2 to 8; and n is an integer of from 3 to 11; with the proviso that m + n is 5 to 19;

15 R¹ is SR⁶, SOR⁶, or SO₂R⁶,

wherein R⁶ is a C₃₋₇cycloalkyl or C₃₋₇cycloalkenyl group;

 R^2 and R^3 are independently selected from hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, halo, phenyl, and C_{1-6} haloalkyl;

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R⁴ and R⁵ are independently selected from hydrogen and C₁₋₄alkyl with the proviso that the total number of carbon atoms in R⁴ and R⁵ is not more than 4;

Ar is a group selected from

and
HO
(d)

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wherein R^8 represents hydrogen, halogen, -(CH₂)_qOR¹¹, -NR¹¹C(O)R¹², -NR¹¹SO₂R¹², -SO₂NR¹¹R¹², -NR¹¹R¹², -OC(O)R¹³ or OC(O)NR¹¹R¹², and R^7 represents hydrogen, halogen, or C₁₋₄ alkyl;

or R⁸ represents -NHR¹⁴ and R⁷ and -NHR¹⁴ together form a 5- or 6- membered heterocyclic ring;

R⁹ represents hydrogen, halogen, –OR¹¹ or –NR¹¹R¹²;

 R^{10} represents hydrogen, halo C_{1-4} alkyl, $-OR^{11}$, $-NR^{11}$ R^{12} , $-OC(O)R^{13}$ or $OC(O)NR^{11}R^{12}$;

 R^{11} and R^{12} each independently represents hydrogen or C_{1-4} alkyl, or in the groups - $NR^{11}R^{12}$, - $SO_2NR^{11}R^{12}$ and - $OC(O)NR^{11}R^{12}$, R^{11} and R^{12} independently represent hydrogen or C_{1-4} alkyl or together with the nitrogen atom to which they are attached form a 5-, 6- or 7- membered nitrogen-containing ring,

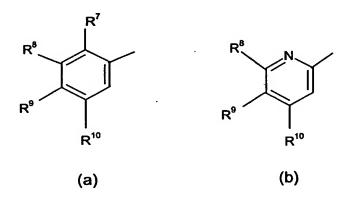
 R^{13} represents an aryl (eg phenyl or naphthyl) group which may be unsubstituted or substituted by one or more substituents selected from halogen, C_{1-4} alkyl, hydroxy, C_{1-4} alkoxy or halo C_{1-4} alkyl; and

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q is zero or an integer from 1 to 4.

- 2. A compound of formula (I) or a salt, solvate of physiologically functional derivative thereof, wherein formula (I) is as defined in claim, except that R⁸ does not represent hydrogen.
- 3. A compound according to claim 1 or claim 2 wherein R¹ represents –SO₂R⁶.
- 4. A compound according to any of claims 1 to 3 wherein R⁶ represents a
 15 C₃₋₇ cycloalkyl group.
 - 5. A compound according to any of claims 1 to 4 wherein R² and R³ each represent hydrogen.
- 20 6. A compound according to any of claims 1 to 5 wherein R⁴ and R⁵ are independently selected from hydrogen and methyl.
 - 7. A compound according to any of claims 1 to 6 wherein Ar is selected from a group (a) or (b):



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8. A compound of formula (la):

5 or a salt, solvate, or physiologically functional derivative thereof, wherein:

m is an integer of from 2 to 8; and n is an integer of from 3 to 11; with the proviso that m + n is 5 to 19;

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R¹ is SR⁶, SOR⁶, or SO₂R⁶, wherein R⁶ is a C₃-rcycloalkyl or C₃-rcycloalkenyl group;

R² and R³ are independently selected from hydrogen, C₁₋₈alkyl, C₁₋₈alkoxy, halo, phenyl, and C₁₋₆haloalkyl; and

 R^4 and R^5 are independently selected from hydrogen and C_{1-4} alkyl with the proviso that the total number of carbon atoms in R^4 and R^5 is not more than 4.

- 20 9. A compound according to any of claims 1 to 8 wherein m is 5 or 6 and n is 3 or 4.
 - 10. A compound of formula (I) or (Ia) selected from:

4-{(1R)-2-[(6-{4-[3-(Cyclopentylsulfinyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol;

- 4-{(1*R*)-2-[(6-{4-[3-(Cyclopentylsulfinyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol (Isomer 1);
 - 4-{(1*R*)-2-[(6-{4-[3-(Cyclopentylsulfinyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol (Isomer 2);
 - 4-{(1R)-2-[(6-{4-[3-(Cyclopentylsulfonyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol;
 - 4-{(1R)-2-[(6-{4-[4-(Cyclopentylsulfonyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol;

4-((1R)-2-{[6-({4-[3-(Cyclohexylsulfonyl)phenyl]butyl}oxy)hexyl]amino}-1-hydroxyethyl)-2-(hydroxymethyl)phenol;

- $4-((1R)-2-\{[6-(4-[3-(3-Cyclopenten-1-ylsulfonyi)phenyi]butyi\}oxy)hexyi]amino}-1-hydroxyethyi)-2-(hydroxymethyi)phenol;$
- 4-((1R)-2-{[6-({5-[3-(Cyclopentylsulfonyl)phenyl]pentyl}oxy)hexyl]amino}-1-hydroxyethyl)-2-(hydroxymethyl)phenol;
 - 4-((1R)-2-{[7-({3-[3-(Cyclopentylsulfonyl)phenyl]propyl}oxy)heptyl]amino}-1-hydroxyethyl)-2-(hydroxymethyl)phenol;
 - 4-((1R)-2-{[6-({4-[3-(Cyclopentylsulfonyl)-5-methylphenyl]butyl}oxy)hexyl]amino}-1-
- 10 hydroxyethyl)-2-(hydroxymethyl)phenol;
 - *N*-[5-((1*R*)-2-{[6-({4-[3-(Cyclopentylsulfonyl)phenyl]butyl}oxy)hexyl]amino}-1-hydroxyethyl)-2-hydroxyphenyl]methanesulfonamide;
 - $4-((1R)-2-\{[6-(4-[3-(Cyclopentylsulfonyl)phenyl]butyl\}oxy)hexyl]amino}-1-hydroxyethyl)-2-fluorophenol;$
- 6-{2-[(6-{4-[3-(Cyclopentylsulfonyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2- (hydroxymethyl)pyridin-3-ol;
 - 5-{(1*R*)-2-[(6-{4-[3-(Cyclopentylsulfonyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-8-hydroxy-3,4-dihydroquinolin-2(1*H*)-one;
 - 5-{(1R)-2-[(6-{4-[3-(Cyclopentylsulfonyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-
- 20 hydroxyphenylformamide:
 - and salts, solvates, and physiologically functional derivatives thereof.
 - 11. A compound of formula (I) or (Ia) which is:
 - 4-{(1R)-2-[(6-{4-[3-(Cyclopentylsulfonyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-
- 25 (hydroxymethyl)phenol;

- or a salt, solvate, or physiologically functional derivative thereof.
- 12. A compound according to any of claims 1 to 11 in the form of a salt formed with an arylsulphonic acid.
- 13. A compound according to any of claim 8, claim 9 or claim 12 which is selected from:
- 4-{(1*R*)-2-[(6-{4-[3-(cyclopentylsulfonyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl) phenol 4-methylbenzenesulfonate;
- 4-{(1R)-2-[(6-{4-[3-(cyclopentylsulfonyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-
- 35 (hydroxymethyl)phenol 4-bromobenzene sulfonate;

4-{(1R)-2-[(6-{4-[3-(cyclopentylsulfonyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol 4-chlorobenzene sulfonate

- $4-\{(1R)-2-[(6-\{4-[3-(cyclopentylsulfonyl)phenyl]butoxy\}hexyl)amino]-1-(1R)-2-[(6-\{4-[3-(cyclopentylsulfonyl)phenyl]butoxy]hexyl)amino]-1-(1R)-2-[(6-\{4-[3-(cyclopentylsulfonyl)phenyl]butoxy]hexyl)amino]-1-(1R)-2-[(6-\{4-[3-(cyclopentylsulfonyl)phenyl]butoxy]hexyl)amino]-1-(1R)-2-[(6-\{4-[3-(cyclopentylsulfonyl)phenyl]butoxy]hexyl)amino]-1-(1R)-2-[(6-\{4-[3-(cyclopentylsulfonyl)phenyl]butoxy]hexyl)amino]-1-(1R)-2-[(6-\{4-[3-(cyclopentylsulfonyl)phenyl]butoxy]hexyl)amino]-1-(1R)-2-[(6-\{4-[3-(cyclopentylsulfonyl)phenyl]butoxy]hexyl)amino]-1-(1R)-2-[(6-\{4-[3-(cyclopentylsulfonyl)phenyl]butoxy]hexyl)amino]-1-(1R)-2-[(6-\{4-[3-(cyclopentylsulfonyl)phenyl]butoxy]hexyl)amino]-1-(1R)-2-[(6-\{4-[3-(cyclopentylsulfonyl)phenyl]butoxy]hexyl)amino]-1-(1R)-2-[(6-\{4-[3-(cyclopentylsulfonyl)phenyl]butoxy]hexyl)amino]-1-(1R)-2-[(6-\{4-[3-(cyclopentylsulfonyl)phenyl]butoxy]hexyl)amino[3-(cyclopentylsulfonyl)phenyl]butoxyl)amino[3-(cyclopentylsulfonyl)pheny$
- hydroxyethyl}-2-(hydroxymethyl)phenol 3-toluene sulfonate;
- 5 4-{(1R)-2-[(6-{4-[3-(cyclopentylsulfonyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2- (hydroxymethyl) phenol 4-biphenyl sulfonate; and
 - 4-{(1R)-2-[(6-{4-[3-(cyclopentylsulfonyl)phenyl]butoxy}
 - hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol, naphthalene-2-sulfonate.
- 10 14. A compound according to claim 13 wherein the salt is in crystalline form.
 - 15. A method for the prophylaxis or treatment of a clinical condition in a mammal, such as a human, for which a selective β_2 -adrenoreceptor agonist is indicated, which comprises administration of a therapeutically effective amount of a compound of formula (I) or (Ia) according to any of claims 1 to 14 or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof.
 - 16. A compound of formula (I) or (Ia) according to any of claims 1 to 14 or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof for use in medical therapy.
 - 17. A pharmaceutical formulation comprising a compound of formula (I) or (Ia) according to any of claims 1 to 14 or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof, and a pharmaceutically acceptable carrier or excipient, and optionally one or more other therapeutic ingredients.
 - 18. A combination comprising a compound of formula (I) or (Ia) according to any of claims 1 to 14 or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof, and one or more other therapeutic ingredients.
 - 19. The use of a compound of formula (I) or (Ia) according to any of claims 1 to 14 or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof in the manufacture of a medicament for the prophylaxis or treatment of a clinical condition for which a selective β_2 -adrenoreceptor agonist is indicated.

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20. A process for the preparation of a compound of formula (I) or (Ia) according to any of claims 1 to 14 or a salt, solvate, or physiologically functional derivative thereof, which comprises:

(a) deprotection of a protected intermediate, for example of formula (II):

$$R^{19}$$
 CHCH₂NR²⁰CR⁴R⁵(CH₂)_m—O—(CH₂)_n— R^2 (II)

or a salt or solvate thereof, wherein R¹, R², R³, R⁴, R⁵, m, and n are as defined for the compound of formula (I), R¹⁹ represents an optionally protected form of Ar; and R²⁰ and R²¹ are each independently either hydrogen or a protecting group, provided that the compound of formula (II) contains at least one protecting group;

(b) reaction of a compound of formula (X):

$$R^{10} - CHCH_{2}NR^{20}CR^{4}R^{5} - (CH_{2})_{m} - O - (CH_{2})_{n}$$

$$R^{10} - CHCH_{2}NR^{20}CR^{4}R^{5} - (CH_{2})_{m} - O - (CH_{2})_{n}$$

$$R^{2} - CH - CHR^{20}$$

$$CH_{2})_{y}CH = CHR^{20}$$

$$R^{3} - CHCH_{2}NR^{20}CR^{4}R^{5} - (CH_{2})_{m} - O - (CH_{2})_{n}$$

$$R^{3} - CHCH_{2}NR^{20}CR^{4}R^{5} - (CH_{2})_{m} - O - (CH_{2})_{n}$$

$$R^{3} - CHCH_{2}NR^{20}CR^{4}R^{5} - (CH_{2})_{m} - O - (CH_{2})_{n}$$

$$R^{3} - CHCH_{2}NR^{20}CR^{4}R^{5} - (CH_{2})_{m} - O - (CH_{2})_{n}$$

$$R^{3} - CHCH_{2}NR^{20}CR^{4}R^{5} - (CH_{2})_{m} - O - (CH_{2})_{n}$$

$$R^{3} - CHCH_{2}NR^{20}CR^{4}R^{5} - (CH_{2})_{m} - O - (CH_{2})_{n}$$

$$R^{3} - CHCH_{2}NR^{20}CR^{4}R^{5} - (CH_{2})_{m} - O - (CH_{2})_{n}$$

$$R^{3} - CHCH_{2}NR^{20}CR^{4}R^{5} - (CH_{2})_{m} - O - (CH_{2})_{m}$$

$$R^{3} - CHCH_{2}NR^{20}CR^{4}R^{5} - (CH_{2})_{m} - O - (CH_{2})_{m}$$

$$R^{3} - CHCH_{2}NR^{20}CR^{4}R^{5} - (CH_{2})_{m} - O - (CH_{2})_{m}$$

$$R^{3} - CHCH_{2}NR^{20}CR^{4}R^{5} - (CH_{2})_{m} - O - (CH_{2})_{m}$$

$$R^{3} - CHCH_{2}NR^{20}CR^{4}R^{5} - (CH_{2})_{m} - O - (CH_{2})_{m}$$

$$R^{3} - CHCH_{2}NR^{20}CR^{4}R^{5} - (CH_{2})_{m} - O - (CH_{2})_{m}$$

$$R^{3} - CHCH_{2}NR^{20}CR^{4}R^{5} - (CH_{2})_{m}$$

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wherein R^2 , R^3 , R^4 , R^5 , R^{19} , R^{20} , R^{21} , m and n are as defined for formula (II) each R^{26} independently represents hydrogen or C_{1-4} alkyl, and x and y each represent 0, 1 or 2; to effect ring closure;

(c) alkylation of an amine of formula (XIII):

wherein R²², R²³, R²⁰ and R²¹ are each independently either hydrogen or a protecting group with a compound of formula (XVII):

$$L^{1}CR^{4}R^{5}(CH_{2})_{m}-O-(CH_{2})_{n}$$
(XVII)

wherein R¹, R², R³, R⁴, R⁵, m, and n are as defined for the compound of formula (I) and L¹ is a leaving group;

(d) reduction of a compound of formula (XIX):

$$R^{18}CHCH_2NR^{20}CR^4R^5(CH_2)_m - O - (CH_2)_{n-2} = R^2$$
 R^1
 $R^{18}CHCH_2NR^{20}CR^4R^5(CH_2)_m - O - (CH_2)_{n-2} = R^3$
 R^3
(XIX)

- Wherein R¹, R², R³, R⁴, R⁵, m and n are as defined for formula (I), R¹⁹ represents an optionally protected form of Ar and R²⁰ and R²¹ are each independently hydrogen or a protecting group as defined above.
 - (e) reacting a compound of formula (XXIII):

wherein R¹⁹ is as hereinbefore defined and L³ is a leaving group as defined above for L¹ or L²;

or a compound of formula (XXIV):

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wherein R¹⁹ is as hereinbefore defined with an amine of formula (XXV):

$$R^{20}HNCR^4R^5(CH_2)_m - O - (CH_2)_n$$
 (XXV)

wherein R1, R2, R3, R4, R5, R20, m and n are as defined for formula (II); or

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(f) removal of a chiral auxiliary from a compound of folrmula (IIa)

$$R^{19}CHCH_2NR^{27}CR^4R^5(CH_2)_m$$
 — O — $(CH_2)_n$ — R^2 R^1 R^3 (IIa)

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wherein $R^1 - R^5$, m and n are as defined for formula (I), R^{19} represents an optionally protected form of Ar, R^{21} represent hydrogen or a protecting group and R^{27} represents a chiral auxiliary.

followed by the following steps in any order:

- (i) optional removal of any protecting groups;
- (ii) optional separation of an enantiomer from a mixture of enantiomers;

(iii) optional conversion of one compound of formula (I) to a different compound of formula (I) eg. conversion of a compound wherein R¹ is SR⁶ to a compound wherein R¹ is SOR⁶ or SO₂R⁶, or conversion of a compound wherein R¹ is SOR⁶ to a compound wherein R¹ is SO₂R⁶;

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- (iv) optional conversion of a compound wherein R⁶ represents cycloalkenyl to a compound wherein R⁶ represents cycloalkyl, eg. by hydrogenation;
- (v) optional conversion of the product to a corresponding salt, solvate, or physiologically functional derivative thereof.

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21. An intermediate selected from a compound of formula (II) (III) (IV) (X) and (XIX) as hereinbefore defined.